**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**
**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

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| In re Application of: | ) | |
| | ) | |
| WOLGAST et al. | ) | Group Art Unit: 1624 |
| | ) | |
| Application No.: 10/560,953 | ) | Examiner: Brenda Libby Coleman |
| | ) | |
| International Filing Date: June 16, 2004 | ) | Confirmation No.: 1700 |
| | ) | |
| 371(c) Date: April 26, 2007 | ) | |
| | ) | |
| For: PROCESS FOR PREPARING 3-BENZAZEPINES | ) | |
| | ) | |

**Attention: Mail Stop Appeal Brief-Patents**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

## APPEAL BRIEF UNDER BOARD RULE § 41.37

Further to Board Rule 41.37, Appellant presents this brief and encloses herewith the fee of $1,345.00 required under 37 C.F.R. § 41.20(b)(2).

This Appeal responds to the January 27, 2011 final rejection of claims 58 and 62-90. An amendment under 37 CFR 1.116 was filed on March 23, 2011 and an advisory action issued March 29, 2011. A Notice of Appeal was filed April 26, 2011. This Appeal Brief is being filed with an accompanying Petition for Extension of Time of 5 months.

## Table of Contents

## I. Real Party In Interest

Arena Pharmaceuticals, Inc. and/or one or more of its wholly owned subsidiaries are the real parties in interest. This application was assigned to Arena Pharmaceuticals, Inc. on April 27, 2007 (recorded at Reel/Frame No. 019199/0555). Arena Pharmaceuticals GmbH, a wholly owned subsidiary of Arena Pharmaceuticals, Inc., has entered into a marketing and supply agreement with Eisai Inc. in the United States.

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## II. Related Appeals and Interferences

There are currently no other appeals or interferences in the United States, of which appellant, appellant's legal representative, or assignee are aware, that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

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## III. Status Of Claims

The status of Appellant's claims is as follows:

Claims 1-57 and 59-61 are cancelled; and

Claims 58 and 62-90 are pending and finally rejected.

*See* Final Office Action dated January 27, 2011 at Office Action Summary (PTOL-326).

The claims on appeal are claims 58 and 62-90 and are reproduced in the attached Claims Appendix.

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## IV. Status Of Amendments

An amendment after the final rejection was filed to correct a typographical error in claim 67, specifically, to delete the word "a". That amendment was not entered by the Office and that amendment is not incorporated into the claims of the Claims Appendix. No amendments are being filed concurrently with this appeal brief.

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## V. Summary Of Claimed Subject Matter

The following summary is not intended to be in any way inconsistent with the express words recited in claims 58 and 62-90. Those claims, with portions highlighted that are particularly relevant to this appeal, are directed to:

> A hydrochloric acid salt of ((*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine;
>
> > (specification at e.g., at line 36, page 59 to line 19, page 60 and in original claim 650)
>
> A **hydrate of a hydrochloric acid salt** of a (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine; or
>
> > (specification at e.g., third paragraph on page 10 of the Application No. 10/41 0,991 ("the '991 application"); see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)
>
> A **solvate of a hydrochloric acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine;
>
> > (specification at e.g., p third paragraph on page 10, in the second paragraph on page 23, and on pages 11-12 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

Other claims are directed to:

> A composition comprising a hydrochloric acid salt, a **hydrate of a hydrochloric acid salt**, or a **solvate of a hydrochloric**

**acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine;

(specification at e.g., second paragraph on page 23 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

A method of treating obesity comprising administering to a patient in need of such treatment a hydrochloric acid salt, a **hydrate of a hydrochloric acid salt**, or a **solvate of a hydrochloric acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine;

(specification at e.g., pages 11-12 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

A method for decreasing food intake in a patient comprising administering to a patient in need thereof a hydrochloric acid salt, a **hydrate of a hydrochloric acid salt**, or a **solvate of a hydrochloric acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine;

(specification at e.g., pages 11-12 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

A method for inducing satiety in a patient comprising administering to a patient in need thereof a hydrochloric acid salt, a **hydrate of a hydrochloric acid salt**, or a **solvate of**

**a hydrochloric acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine;

(specification at e.g., pages 11-12 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

A method for controlling weight gain in a patient comprising administering to a patient in need thereof a hydrochloric acid salt, a **hydrate of a hydrochloric acid salt**, or a **solvate of a hydrochloric acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine; and

(specification at e.g., pages 11-12 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

A method for the management of obesity in a patient comprising administering to a patient in need thereof a hydrochloric acid salt, a **hydrate of a hydrochloric acid salt**, or a **solvate of a hydrochloric acid salt** of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine, including wherein the management of obesity comprises a method for decreasing body weight, or a method for maintaining weight and further wherein the patient has an initial body mass index of greater than 30 $kg/m^2$.

(specification at e.g., pages 11-12 of the '991 application and pages 1-2 of the '991 application; see, also response filed November 17, 2010, wherein the specification was amended to incorporate that portion of the '991 application, which had been incorporated by reference)

## VI. Grounds of Rejection

There are three grounds of rejection against the appealed claims.

- Claims 67 and 72-90 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salt forms, allegedly does not reasonably provide enablement for solvates and hydrates.

- Claims 58 and 62-90 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 and 41-46 of copending Application No. 11/793,473.

- Claims 58 and 62-90 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/599,050, now U.S. Patent No. 7,977,329.

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## VII. Argument

A. The Claims Are Enabled

Claims 67 and 72-90 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salt forms, allegedly does not reasonably provide enablement for solvates and hydrates. Specifically, the Office states that applicants "must show that solvates and hydrates can be made, or limit the claims accordingly." Final Office Action, mailed January 27, 2011, at page 6.. In the Advisory Action mailed March 29, 2011, the Office further comments that "an application must be enabling as of the filing date and not at a date later than the filing of the application." Appellants submit that the application as filed is enabled and that the post-filing date data supplied to the Office simply serves to confirm the enablement of the application.

As discussed above, the pending claims relate to a hydrochloric acid salt of (R)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine, a solvate of that hydrochloric acid salt, such as a hydrate of that hydrochloric acid salt, and compositions and methods of use thereof. The formation of solvates, including hydrates, was not a nascent technology at the time the application was filed. Rather, as of the filing date for the subject application, the literature was replete with examples of methods for formation of solvates, including hydrates. For example, U.J. Griesser, *Polymorphism in the Pharmaceutical Industry,* ed. Rolf Hilfiker, Wiley-VCF Verlag GmbH & Co. Weinheun, Germany 2006:

> Often, solvates can simply and quickly be generated by suspending the substance in the solvent or by wetting and grinding. Vapor sorption is a common method to generate hydrates. Exposure of a specific polymorph to water vapor may even result in a metastable hydrate form. Griesser, at page 223.

In addition, referring to K.J. Guillory, *Polymorphism in Pharmaceutical Solids,* ed. Harry G. Brittan, Vol. 95, Marcel Dekker, Inc. NY, 1999:

> Pharmaceutical solids may come into contact with water during processing steps, such as crystallization,

> lyophilization, wet granulation, aqueous film coating, or spray-drying. Moreover, they may be exposed to water during storage in an atmosphere containing water vapor, or in a dosage form consisting of materials that contain water (e.g., excipients) and are capable of transferring it to other ingredients. Water may be adsorbed onto the solid surface and/or may be absorbed in the bulk solid structure. When water is incorporated into the crystal lattice of the compound in stoichiometric proportions, the molecular adduct or adducts formed are referred to as hydrates. [... ] Simply exposing an anhydrous powder to high relative humidity can often lead to formation of a hydrate. Guillory, at pages 202 and 204.

Furthermore, in some cases, a compound preferentially exists as a hydrate, and an anhydrous form will spontaneously absorb water to form the hydrate:

> The stabilizing and protecting role of water in crystalline hydrates is well known for a series of β-lactam antibiotics. Cefixime trihydrate is a very intriguing example. The partially dehydrated hydrate becomes disordered, which enables a hydrolytic reaction. Although *the anhydrous form is chemically stable* it cannot be used because *it readily picks up water and rehydrates on storage*. [... ] Similar reports exist of ampicillin trihydrate. Griesser, at page 226, emphasis added.

Appellants thus maintain that the literature as of the filing date of the subject application shows that solvates, including hydrates, were obtained routinely.

Appellants submit that the hydrochloric acid salt of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine possesses the property of readily forming solvates, including hydrates. Furthermore, the specification indicates that "[t]he compounds of this invention may form solvates with standard low molecular weight solvents using methods known to the skilled artisan." See, Response filed November 17, 2010. And as confirmed by the post-filing date data provided by Appellants, solvates, including hydrates, of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine were readily prepared. See, WO 2006/069363 (page 16, Example 2). Appellants also refer the

Office to WO 2007/120517 (pages 27-29, Example 4), which shows that an anhydrous hemitartrate salt of 8-chloro-1-methyl-2,3,4,5-tetrahydro-1H-benzazepine is converted to a hemihydrate hydrochloric acid salt with a water content of about 3.7% by weight. That also demonstrates that a hydrate of a salt exists.

Finally, Appellants note that the Board of Patent Appeals and Interferences has repeatedly recognized that claims to solvates are indeed patentable, even in the absence of working examples. Indeed, ***every time that the Board has faced this issue, the Board has found that the claims to hydrates or solvates are enabled and satisfy the written description requirement.*** See, for example, the following decisions:

- *Ex parte Germeyer et al.*, Appeal 2010-005038, Application No. 10/891,554 (stating that claims to hydrates satisfy the written description and enablement requirements; that such claims do not require a hydrate having a specific structure and do not require that a hydrate structure be identified; and that hydrates form naturally, whether their structures can be predicted in advance or not;
- *Ex parte Liu and Zhao*, Appeal 2009-015302, Application 10/820,647 (BPAI, 09/17/2010) (stating that "the Examiner has overemphasized the importance of working examples, and given 'too little credit to the abilities of a person having ordinary skill in the art'" (citations omitted));
- *Ex Parte Gante et al.*, Appeal No. 2000-0600, Application No. 08/642,268 (BPAI, 05/06/2002); and
- *Ex parte Singh et al.*, Appeal 2010-003085, Application No. 10/931,481.

Appellants have thus shown that solvates, including hydrates, can be made using techniques well known in the art at the time of filing.[1] Furthermore, the Board's own

[1] In addition, all arguments made previously in response to the Office's rejection under 35 U.S.C. § 112, first paragraph, are repeated and maintained herein. Appellants reserve the right to rely upon these arguments in further proceedings.

decisions fully support the patentability of the subject application. Appellants submit that the claims are fully enabled and request that the rejection be withdrawn.

B. The Obviousness-type Double Patenting Rejections Should be Withdrawn

1. Copending Application No. 11/793,473

Claims 58 and 62-90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-31 of copending Application No. 11/793,473 ("the '473 application").

Pursuant to MPEP 804(B)1, if a provisional nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of the two pending applications, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer. Appellants submit that the instant application, which was filed on June 16, 2004, was filed earlier than the '473 application, which was filed as a national stage application of PCT/US2005/046983 filed on December 20, 2005. Therefore, Appellants will not address the merit of the provisional obviousness double patenting rejection but request that the subject application be allowed to issue without a terminal disclaimer upon withdrawal of the other rejections.

2. Copending Application No. 11/599,050

Claims 58 and 62-90 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/599,050, now U.S. Patent No. 7,977,329. Accordingly, while acknowledging the rejection, Appellants request that the rejection be held in abeyance until such time as when allowable claims are identified.

## VIII. Conclusion

It is respectfully submitted that the reasons given above claims 58 and 62-90 are allowable. Reversal of the Examiner's rejections is respectfully requested.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to Deposit Account 19-0741.

Respectfully submitted,

Date 11-15-11 By _____

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## IX. Claims Appendix to Appeal Brief Under Rule 41.37(c)(1)(viii)

1. - 57. (Cancelled).

58. A composition comprising a hydrochloric acid salt according to claim 66.

59. - 61. (Cancelled).

62. A method for treating obesity comprising administering to a patient in need of such treatment a hydrochloric acid salt according to claim 66.

63. A method for decreasing food intake in a patient comprising administering to a patient in need thereof a hydrochloric acid salt according to claim 66.

64. A method for inducing satiety in a patient comprising administering to a patient in need thereof a hydrochloric acid salt according to claim 66.

65. A method for controlling weight gain in a patient comprising administering to a patient in need thereof a hydrochloric acid salt according to claim 66.

66. A hydrochloric acid salt of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine.

67. A hydrate of a hydrochloric acid salt of a (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine.

68. A method for the management of obesity in a patient comprising administering to a patient in need thereof a hydrochloric acid salt according to claim 66.

69. The method according to claim 68, wherein said method for the management of obesity comprises a method for decreasing body weight.

70. The method according to claim 68, wherein said method for the management of obesity comprises a method for maintaining weight.

71. The method according to claim 68, wherein said patient has an initial body mass index of greater than 30 $kg/m^2$.

72. A composition comprising a hydrate of a hydrochloric acid salt according to claim 67.

73. A method for treating obesity comprising administering to a patient in need of such treatment a hydrate of a hydrochloric acid salt according to claim 67.

74. A method for decreasing food intake in a patient comprising administering to a patient in need thereof a hydrate of a hydrochloric acid salt according to claim 67.

75. A method for inducing satiety in a patient comprising administering to a patient in need thereof a hydrate of a hydrochloric acid salt according to claim 67.

76. A method for controlling weight gain in a patient comprising administering to a patient in need thereof a hydrate of a hydrochloric acid salt according to claim 67.

77. A method for the management of obesity in a patient comprising administering to a patient in need thereof a hydrate of a hydrochloric acid salt according to claim 67.

78. The method according to claim 77, wherein said method for the management of obesity comprises a method for decreasing body weight.

79. The method according to claim 77, wherein said method for the management of obesity comprises a method for maintaining weight.

80. The method according to claim 77, wherein said patient has an initial body mass index of greater than 30 $kg/m^2$.

81. A solvate of a hydrochloric acid salt of (*R*)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine.

82. A composition comprising a solvate of a hydrochloric acid salt according to claim 81.

83. A method for treating obesity comprising administering to a patient in need of such treatment a solvate of a hydrochloric acid salt according to claim 81.

84. A method for decreasing food intake in a patient comprising administering to a patient in need thereof a solvate of a hydrochloric acid salt according to claim 81.

85. A method for inducing satiety in a patient comprising administering to a patient in need thereof a solvate of a hydrochloric acid salt according to claim 81.

86. A method for controlling weight gain in a patient comprising administering to a patient in need thereof a solvate of a hydrochloric acid salt according to claim 81.

87. A method for the management of obesity in a patient comprising administering to a patient in need thereof a solvate of a hydrochloric acid salt according to claim 81.

88. The method according to claim 87, wherein said method for the management of obesity comprises a method for decreasing body weight.

89. The method according to claim 87, wherein said method for the management of obesity comprises a method for maintaining weight.

90. The method according to claim 87, wherein said patient has an initial body mass index of greater than 30 $kg/m^2$.

## X. Evidence Appendix to Appeal Brief Under Rule 41.37(c)(1)(ix)

U. J. Griesser, *Polymorphism in the Pharmaceutical Industry,* ed. Rolf Hilfiker, Wiley-VCF Verlag GmbH & Co. Weinheun, Germany 2006, submitted by Applicant in an Information Disclosure Statement on June 8, 2010 and initialed by the Examiner on August 17, 2010.

WO 2006/069363, submitted by Applicant in an Information Disclosure Statement on June 8, 2010 and initialed by the Examiner on August 17, 2010.

WO 2007/120517, submitted by Applicant in an Information Disclosure Statement on June 8, 2010 and initialed by the Examiner on August 17, 2010.

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## XI. Related Proceedings Appendix to Appeal Brief Under Rule 41.37(c)(1)(x)

None.